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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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IKUO MATSUI

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EXAMINER

MONSHIPOURI, MARYAM

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/369,735

Applicant(s)

MATSUI ET AL.

Examiner

Maryam Monshipouri

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-11 and 14-33 is/are pending in the application.
- 4a) Of the above claim(s) 3-7, 25-27 and 32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 8-11, 14-24, 28-31 and 33 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ | 6) <input type="checkbox"/> Other: ____ |

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Applicant's response to restriction requirement filed 10/16/2003 is acknowledged. Applicant elected Group IIa invention directed to claims 8-11, 14-24, 28-31 and 33 without traverse. Claims 3-7, 25-27, 32 are withdrawn, as drawn to non-elected inventions. Claims 1-2, 12-13, are canceled.

DETAILED ACTION

Claims 8-11, 14-24, 28-31 and 33 are under examination on the merits.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 8-11 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP 2172.01. The omitted steps are: contacting the enzyme with β -glycoside etc in claim 8. Claims 9-11 are rejected for depending from a rejected base claim.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 8-11, 28-30 and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of use of SEQ

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ID NO:2 , does not reasonably provide enablement for methods of use of tetramers of variants of SEQ ID NO:2 wherein plurality of amino acid residues are deleted, replaced or added, or wherein said variants are encoded by DNA sequences that can hybridize to SEQ ID NO:1 under wash temperatures of 25°C , or 55°C.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2n 1400 (Fed. Cir. 1988) are: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

With respect to claims 8-11, the specification does not teach or explain up to how many amino acid residues in SEQ ID NO:2 may be deleted, replaced or added before said monomer fails to form a tetramer enzyme and therefore said enzyme loses its appropriate confirmation and activity. No examples of SEQ ID NO:2 variants are provided either. Current state of the art indicates that if , for example, 100 amino acids are randomly deleted from or added to SEQ ID NO:2 said product is unlikely to form a tetramer that retains its appropriate three dimensional structure in order to hydrolyze β glycoside. Therefore due to lack of sufficient teachings and examples provided in the specification and due to unpredictability of prior art as to up to how many residues in SEQ ID NO:2 may be mutated before said polypeptide loses its ability to form a tetramer with activity one of skill in the art has to go through the burden of undue

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experimentation in order to screen for SEQ ID NO:2 variants and their tetramers which can be used in methods of claim 8-11 and as such the claims go beyond the scope of the disclosure.

With respect to claims 28-30, and 33 applicant is well ware that a DNA sequence that can hybridize to SEQ ID NO:1 under broad wash conditions of 25°C or 55°C is most likely capable of encoding a variant of SEQ ID NO:2 which can no longer form an appropriate β -glycosidase tetramer with activity..

The specification does not teach which critical residues in DNA sequences that hybridize to SEQ ID NO:1 under wash conditions recited in claims 28, 30, and 33 must be retained such that their expression products retain a structure that can form a tetramer with β -glycosidase activity. NO examples of the expression products of such DNA sequences are provided either. Current state of the art indicates that any DNA sequence that happens to hybridize to a sequence that can encode a full-length enzyme monomer (such as β -glycosidase monomer) is not necessarily capable of encoding a product which can form a tetramer which retains the appropriate structure and thereby activity.

Therefore, due to lack of sufficient examples and guidance provided in the specification and due to unpredictability of prior art as to which residues in DNA sequences that can hybridize to that encoding a useful polypeptide, under wash conditions of claims 28, 30 and 33, such that their expression products retains the

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appropriate conformation to form a tetramer, which retains beta glycosidase activity one of skill in the art has to go through the burden of undue experimentation in order to use the SEQ ID NO:2 variants that are within the scope of this invention and as such the claims are not fully enabled.

5. Claims 8-11, 28-30 and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 8 (and its dependent claims 9-11), claim 28 (and its dependent claim 29), claims 30 and 33 are directed to methods of use of a **genera** of β -glycosidase tetramers prepared from variants of SEQ ID NO:2, wherein said variants are either obtained by creating plurality of mutations of SEQ ID NO:2 or obtained by expressing sequences that hybridize to SEQ ID NO:1, under conditions recited in claims 28, 30 or 33 and reconstituting said variants, wherein said genera have been inadequately described in the specification.

The specification does not contain any disclosure of the structure of all sequences that are variants of SEQ ID NO:2 that can be reconstitute to form an active tetramer. The genera of claimed polypeptides are large variable genera with the potentiality of reconstituting products that have nothing to do with claimed beta-glycosidase. Therefore, many functionally unrelated polypeptides (variants) are

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encompassed within the scope of these claims. The specification discloses only a **single species** of the claimed genera (SEQ ID NO:2) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Since claimed enzyme variants are not adequately described their method of use are not adequately described either.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 8-11, 14-24, 28-31 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawarabayasi et al. (DNA Res., 5, 55-76, 1998, cited previously) in view of Current enzyme assay techniques. As mentioned previously,

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Kawarabayasi teaches a beta glucosidase from *Pyrococcus horikoshii* where each subunit of which has 100% identity to SEQ ID NO:2 of this invention. Kawarabayasi does not teach a method of use of said enzyme in an enzyme assay for hydrolysis of β -glucoside.

Current enzyme assay techniques teach that once a potential enzymatic activity for a protein is found, said protein can be solubilized and contacted with its potential substrate under appropriate reaction conditions in order to confirm the potential activity of said protein.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to start with the polypeptide of Kawarabayasi and try to solubilize and assay its activity using a β -glucoside comprising for example a long alkyl chain of 8 or more carbon atoms at temperatures around 100°C, as a substrate, according to current enzyme assay techniques.

One of ordinary skill in the art is motivated in assaying the enzyme of kawarabayasi because said assay confirms the predicted function of said protein as a biocatalyst, practically. Finally, one of ordinary skill in the art has a reasonable expectation of success in performing an assay of said enzyme because methods of assaying glucosidases are fully established in the prior art, rendering the invention obvious.

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Maryam Monshipouri, Ph.D. whose telephone number is (703) 308- 1083.

The Examiner can normally be reached daily from 8:30 A.M. to 5:00 P.M. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. P. Achutamurthy, can be reached at (703) 308-3804. The OFFICIAL fax number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.


MARYAM MONSHIPOURI, PH.D.
PRIMARY EXAMINER